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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,701	11/21/2003	John M. Williams	2478.2017-001	1350

21005 7590 11/09/2005

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	**PAPER NUMBER**
1614	

DATE MAILED: 11/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,701	WILLIAMS, JOHN M.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement (IDS) submitted on July 12, 2004, has been considered.

Claim Rejections - 35 USC § 112

Claims 1 and 7-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 7-11 where $R^{n'}$ is a substituted or unsubstituted alkyl/aralkyl/aryl group are indefinite connoting no information as to what substituents are used, therefore, examiner suggests using substituents selected from ..... groups from the specification.

Claim 8 recites substituted and optionally substituted cycloalkyl, aryl, C_1-C_4 aralkyl and cycloalkylalkyl groups, but surely, they do not all carry the same properties. Therefore, examiner suggests applicant clearly states the compounds or groups that are considered and use the above suggestion supra for the substituted R^n.

Claim 8 recites the limitation "aralkyl" in line 3. There is insufficient antecedent basis for this limitation in the claim 1.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

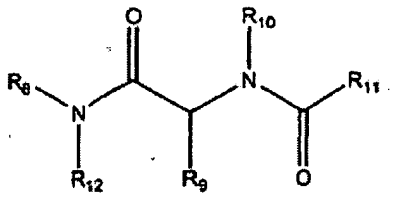
unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim1-20 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-26 of copending Application No. 10/719,055. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: The claims are drawn to a composition and method of inhibiting rejection of a transplant organ composition, using formula



in the instant claim with rapamycin or CD40L. The only difference between the instant application and the co-pending application is in the instant claim adjuvant therapy is used while the co-pending claims treat the condition

with only the compound of formula I. Thus the claims of the instant application are within the scope of the co-pending application.

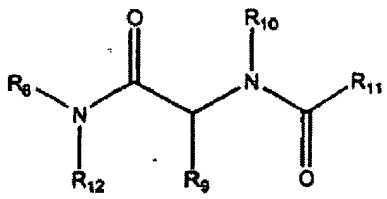
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-16 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sneddon et al., WO 01/87849 and Caine, EP 0401747, in view of Hancock et al., Proc. Natl. Acad.

Sneddon et al., teach, instant claims 1, in part, and 7-14 wherein a structural



formula at page 4 as . The constituents of the R moieties are the same as that claimed by applicant in claims 1 (in part), 7-14 and claim 15 (in part) at pages 10-12. Further, graft versus host disease (transplant) is recited at page 14, line 30, and present claims 2 and 4 as skin/tissue transplant at page 14, line 30, in a mammal. Although the above reference did not per se teach inhibition of rejection of transplanted organ, as claimed by applicant in claim 1, the reference, however, teaches at pages 2 and 3 and 14 that:

> High levels of TNF-α are generally associated with chronic immune or inflammatory diseases, and are considered a cause of neural and cellular degeneration. At lower levels, however, TNF-α plays an important role in the cell life cycle, cellular response to foreign attack, and maintenance of homeostasis. For this reason, it will be appreciated that the purpose of this invention is not the complete and absolute inhibition of TNF-α, but rather the modulation of the cellular response to TNF-α levels and the treatment of TNF-α mediated conditions, thereby permitting an effective treatment for the chronic immune and inflammatory responses that occur when excess TNF-α is produced.
>
> The present compounds can be administered to a patient having a TNF-α mediated medical condition, for example, to inhibit the development of the condition, to inhibit its further progression, and/or to ameliorate the symptoms associated with the condition.

Subsequently, the subject matter of claim 20 is addressed.

Since these compounds are modulators of (tumor necrosis factor) TNF-α signaling, it would therefore have been obvious for one of ordinary skill in the art to use the compounds at pages 4, 10 and 86 for the inhibition rejection of a transplant organ where in the transplant is a graft.

Caine teaches the immunosuppressive agent rapamycin, as in current claims 5 and 6, at page 3, line 11, wherein an effective amount of rapamycin inhibits organ or tissue transplant rejection in mammal at page 3, lines 10-14, wherein the transplanted organ is the liver at page 3 line 47 (current claim 2 and 16).

caine teaches the immunosuppressive agent rapamycin as in current claim 18 at page 3 line 11.

Hancock teaches the CD40L ligand as a member of TNF and its implication in graft rejection. See abstract, wherein treatment with CD40L induces long-term graft survival (abstract) and also at page 13970 (left col.) where anti-CD40L treatment prevented acute cardiac rejection.

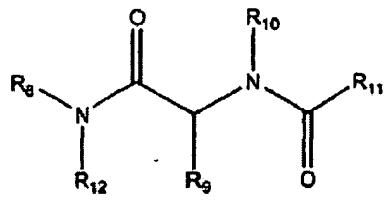
From the above cited references, one of ordinary skill in the art would have been motivated to combine the teachings of Snedden and Caine in view of Hancock, and expect a successful result. Both drugs CD40L and the compound of formula I have been used as immunosuppressive agents ie., for inhibition of organ transplant rejection in patients. Both drugs are modulators of TNF and the above references teach positive results with the use of these compounds.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

With regard to claims 17-19

Claims 17-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sneddon et al., WO 01/87849 and 6,159,938 and Roy, EP 0401747 in view of Hancock et al., Proc. Natl. Acad.

Sneddon et al., teach the compounds in claims 17 and 19 a structural formula at



page 4 as where the constituents of the R moieties are the same as that claimed by applicant in claims 17, 19, 10-12.

Caine teaches, the immunosuppressive agent, rapamycin, as in current claims 5 and 6 at page 3 line 11, wherein an effective amount of rapamycin inhibits organ or tissue transplant rejection in mammal at page 3 lines 10-14, wherein the transplanted organ is the liver at page 3 line 47 (current claim 2 and 16).

Hancock teaches CD40L as the immunosuppressive agent.

Although he above references together did not teach, the combination as claimed by applicant, however, Roy teaches combination of rapamycin with one or more other therapeutic agent for inhibiting transplant rejection at page 3 line 50+.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Sneddon and Caine with that of Hancock, administer an effective amount the drug of Snedden combined with the drug of Caine to inhibit rejection of a transplanted organ in a patient in need thereof.

• From the above cited references, one of ordinary skill in the art would have been motivated to combine the teachings of Snedden, and Caine, in view of Hancock, and expect a successful result. Both drugs CD40L and the compound of formula I have been used for as immunosuppressive agents, and are well know in the art of transplant.

Thus, the claimed invention was prima facia obvious to make and use at the time it was made.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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SVG
10/25/05

Phyllis Spivack

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PRIMARY EXAMINER